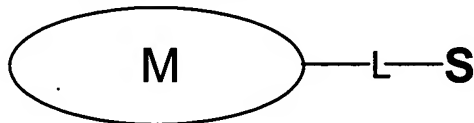


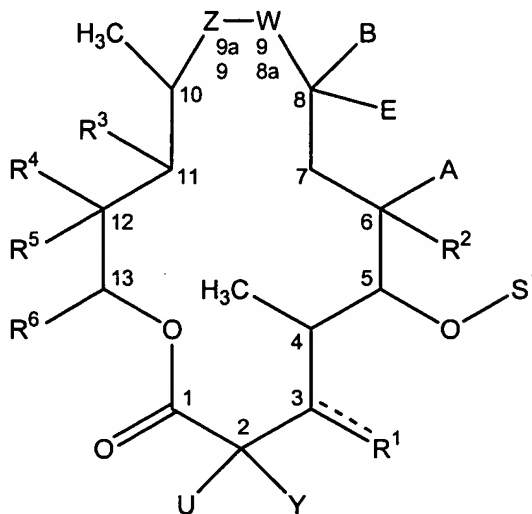
AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A compound of the formula:



I

wherein **M** represents a group of Formula II:



II

wherein

(i) Z and W independently are $>C=O$, $>CH_2$, $>CH-NR_tR_s$, $>N-R_N$ or $>C=N-R_M$, wherein

R_t and R_s independently are hydrogen or alkyl;

R_M is hydroxy, alkoxy, substituted alkoxy or OR^p;

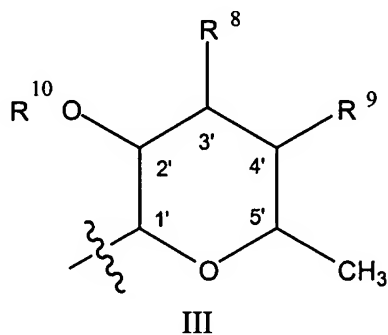
R_N is hydrogen, R^P, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or -C(X)-NR_tR_s; wherein X is =O or =S;

provided that Z and W cannot both simultaneously be, >C=O, >CH₂, >CH-NR_iR_s, >N-R_N, >C=N-R_M or a bond;

(ii) U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;

(iii) R¹ is hydroxy, OR^p, -O-S² group or an =O;

(iv) S¹ is a sugar moiety of Formula III:



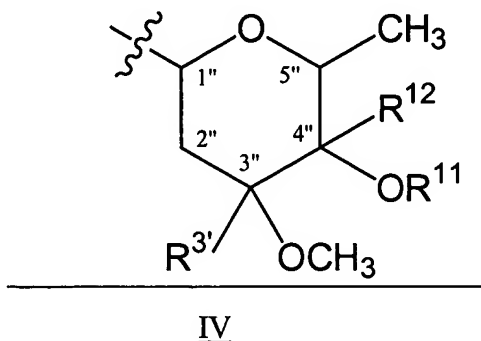
wherein

R⁸ and R⁹ are both hydrogen or together form a bond, or R⁹ is hydrogen and R⁸ is -N(CH₃)R^y, wherein

R^y is R^p, R^z or -C(O)R^z, wherein R^z is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with C₂-C₇-alkyl, C₂-C₇-alkenyl, C₂-C₇-alkynyl, aryl or heteroaryl;

R^{10} is hydrogen or R^p ;

S² sugar moiety of Formula IV:



wherein

R^{3'} is hydrogen or methyl;

R¹¹ is hydrogen, R^p, or O-R¹¹ is a group that with R¹² and with C/4" carbon atom forms a >C=O or epoxy group;

R¹² is hydrogen or a group that with O-R¹¹ group and with C/4" carbon atom forms a >C=O or epoxy group;

(vi) R² is hydrogen, hydroxy, OR^p or alkoxy ;

(vii) A is hydrogen or methyl;

(viii) B is methyl or epoxy;

(ix) E is hydrogen or halogen;

R³ is hydroxy, OR^p, alkoxy or R³ is a group that with R⁵ and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate, or if W or Z is >N-R_N R³ is a group that with W or Z forms a cyclic carbamate;

(xi) R⁴ is C₁-C₄ alkyl;

(xii) R⁵ is hydrogen, hydroxy, OR^p, C₁-C₄ alkoxy, or a group that with R³ and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;

(xiii) R^6 is hydrogen or C_1 - C_4 -alkyl;

wherein M has a linkage site through which it is linked to S via linking group L; provided that the linkage site being at one or more of the following:

a) any reactive hydroxy, nitrogen, or epoxy group located on S¹, S², or an aglycone oxygen if S¹ and/or S² is cleaved off;

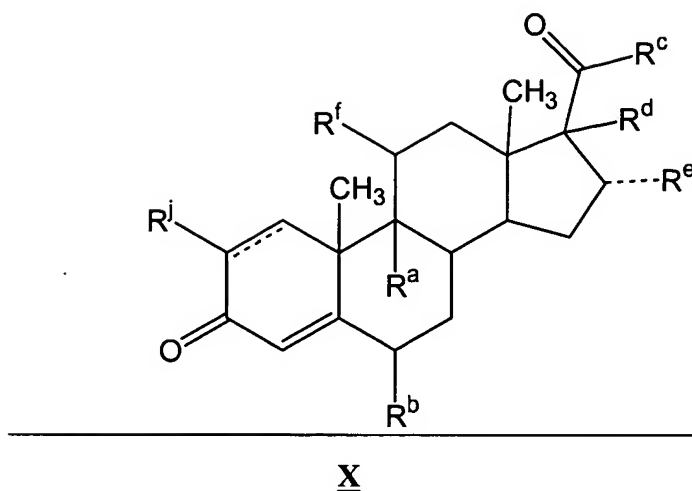
b) a reactive >N-R_N or -NR_tR_s or oxo group located on Z or W;

c) a reactive hydroxy group located at any one of R¹, R², R³, and R⁵;

d) any other group that can be first derivatized to a hydroxy or -NR_iR_s group and

R^p is hydroxyl or amino protective group

S represents a group of Formula X:



wherein

R^a and R^b independently represents, hydrogen or halogen;

R^c is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;

R^d and R^e independently represents: hydrogen, hydroxy, methyl or C₁-C₄-alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

R^f is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

R^j is hydrogen or halogen;

or a pharmaceutically acceptable salt or solvate thereof;

wherein

~~(i) M is a macrolide subunit selected from the group consisting of multi-member lactonic ring molecules, wherein "member" refers to the number of carbon atoms or heteroatoms in the lactonic ring and "multi" signifies a whole number greater than about 10, and up to about 18 said molecules having the property of accumulating within mammalian, including human, immune system cells that mediate inflammatory immune responses;~~

~~(ii) S is a steroidal anti-inflammatory subunit; and~~

OC(O)NH-;

$$-\text{C}(\text{O})\text{NH}_2$$

X² is -NH- or -NHC(O)- or -CH₂-;

Q is -NH- or -CH₂-, wherein

each -CH₂- or -NH- group may be optionally substituted by C₁-C₇-alkyl,

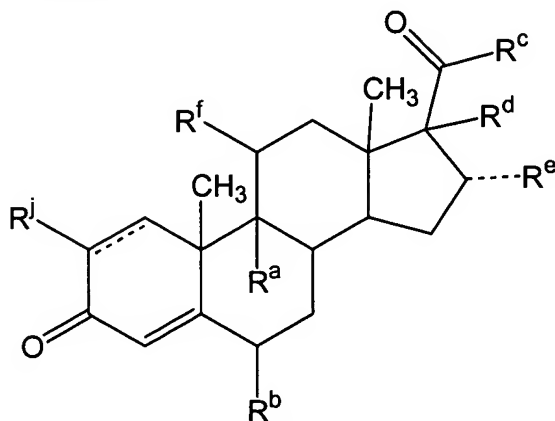
C₂-C₇-alkenyl, C₂-C₇-alkynyl, C(O)R^x, C(O)OR^x, C(O)NHR^x, wherein

R^x may be C₁-C₇-alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 8, with

the proviso that if Q is NH, n cannot be 0;

S represents a group of Formula X:



X

wherein

R^a and R^b independently represents, hydrogen or halogen;

R^c is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;

R^d and R^e independently represents: hydrogen, hydroxy, methyl or C₁-C₄-alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

R^f is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

provided that the linkage is through the nitrogen of Z at N/9a position or through the oxygen of R³ at C/11 position.

6. (Currently amended) The compound according to claim 2 wherein Z is ~~selected~~ selected from >N-H, >N-CH₃, >N-C(O)NHR^x, wherein R^x is isopropyl;
W is >C=O or >CH₂ provided that when Z is >N-CH₃ W cannot be >C=O;
B is methyl;
E is hydrogen;
A is methyl;
R² is hydroxy or methoxy;
S¹ group represents a group of Formula III wherein R⁸ is selected from: amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino; R⁹ and R¹⁰ are hydrogen;
R¹ is O-S² wherein S² represents a group of Formula IV wherein R¹¹ is hydrogen or O-R¹¹ is a group that with R¹² and with C/4"carbon atom forms a >C=O or epoxy group; R¹² is hydrogen or a group that with O-R¹¹ group and with C/4"carbon atom forms a >C=O or epoxy group; R¹³ is methyl;
U is hydrogen;
Y is methyl;
R³ is hydroxy;
R⁴ is methyl;
R⁵ is hydroxy or methoxy;
R⁶ is ethyl;
provided that the linkage is through the nitrogen of R⁸ at C/3', through the oxygen of R² at C/6 or through the carbon of R¹² or through the oxygen of R¹¹ both at C/4".

7. (Currently amended) The compound according to claim [4] 2

wherein

R^a and R^b independently represents, hydrogen or halogen;

R^d is hydrogen or hydroxy;

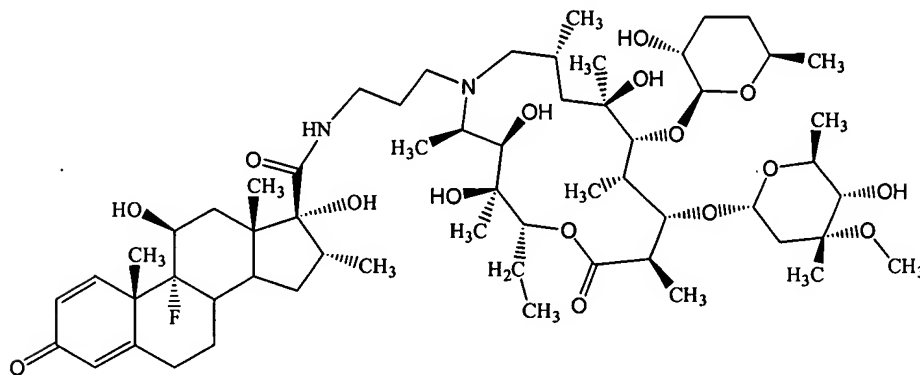
R^e is methyl;

R^f is hydroxy;

R_j is hydrogen

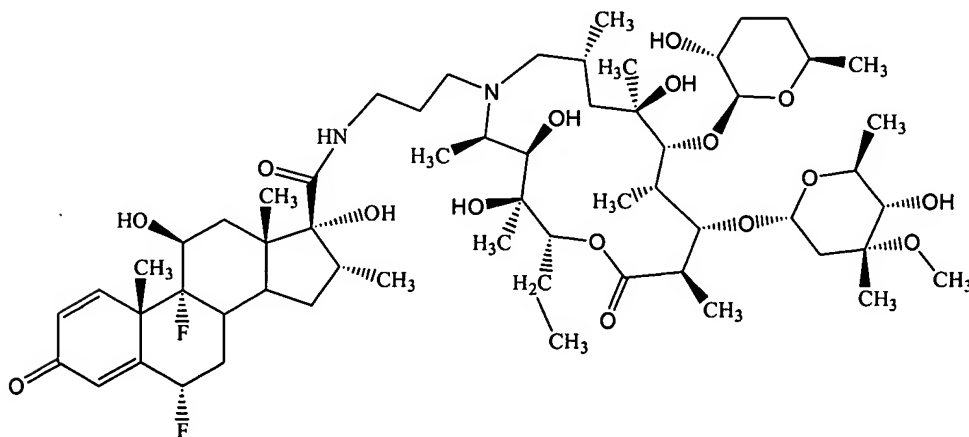
provided that the linkage is through the valence bond R^k .

8. (Currently amended) A compound of the formula



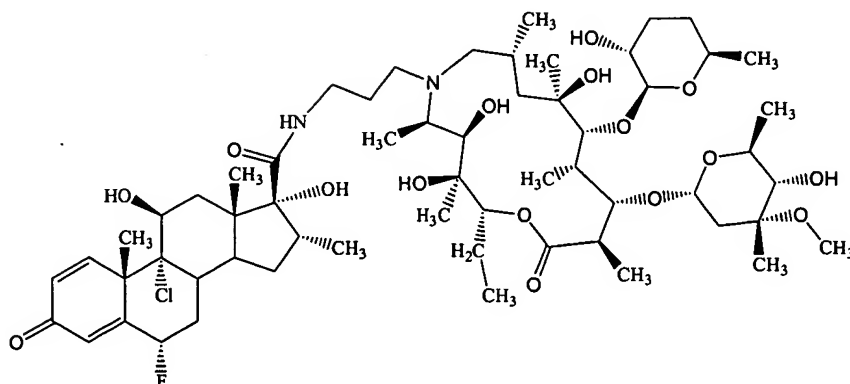
and pharmaceutically acceptable salts and solvates thereof.

9. ((Currently amended) A compound of the formula



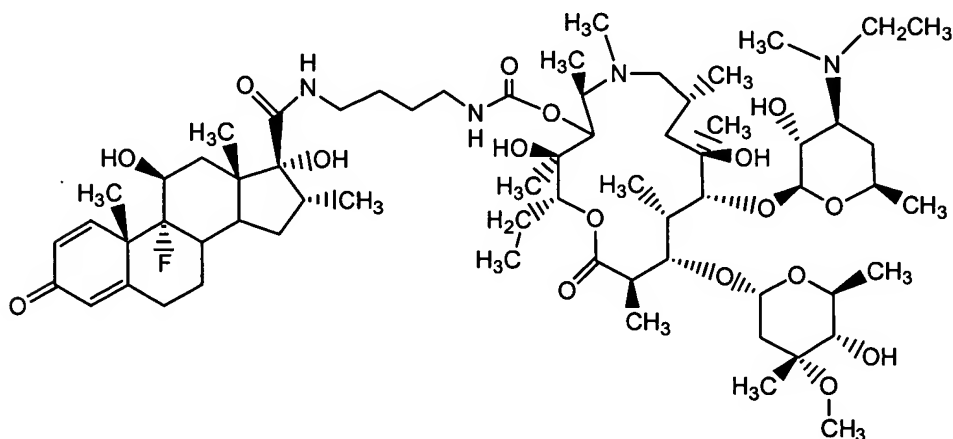
and pharmaceutically acceptable salts and solvates thereof.

10. (Currently amended) A compound of the formula



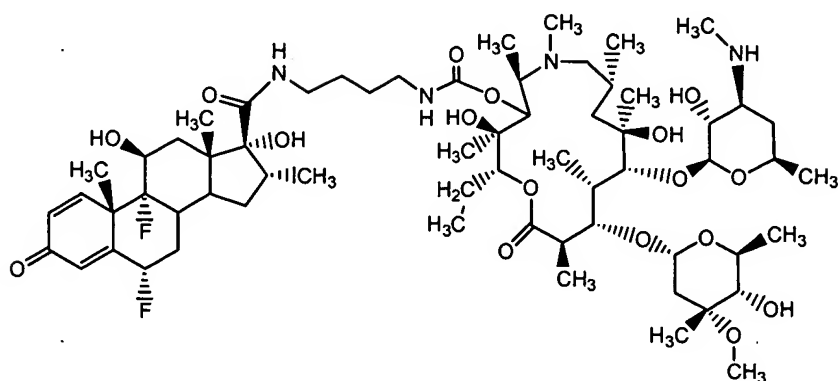
and pharmaceutically acceptable salts and solvates thereof.

11. (Currently amended) A compound of the formula



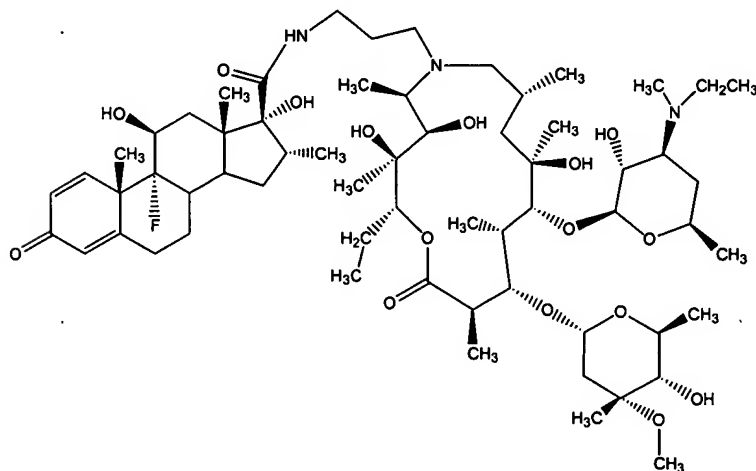
and pharmaceutically acceptable salts and solvates thereof.

14. (Currently amended) A compound of the formula



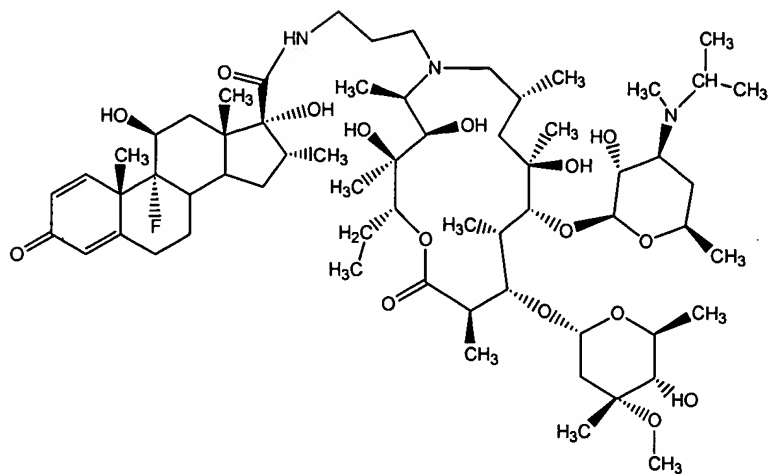
and pharmaceutically acceptable salts and solvates thereof.

15. (Currently amended) A compound of the formula



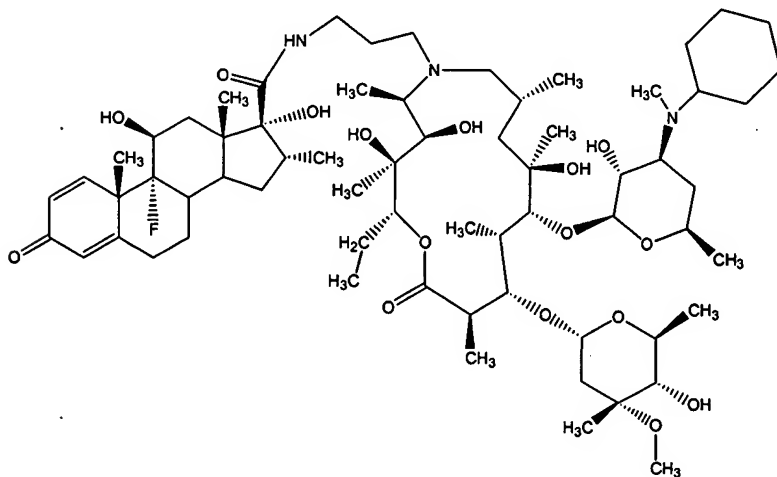
and pharmaceutically acceptable salts and solvates thereof.

18. (Currently amended) A compound of the formula



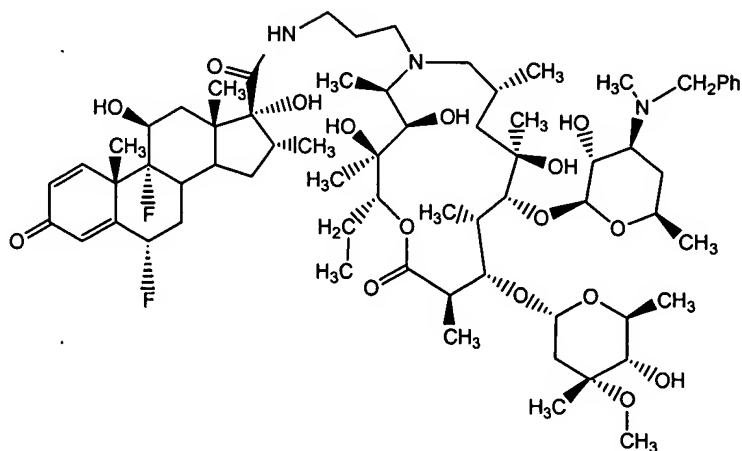
and pharmaceutically acceptable salts and solvates thereof.

19. (Currently amended) A compound of the formula



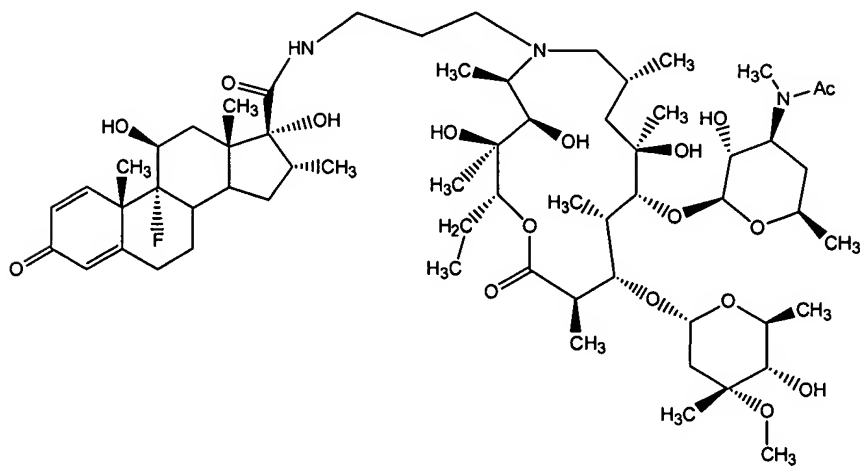
and pharmaceutically acceptable salts and solvates thereof.

20. (Currently amended) A compound of the formula



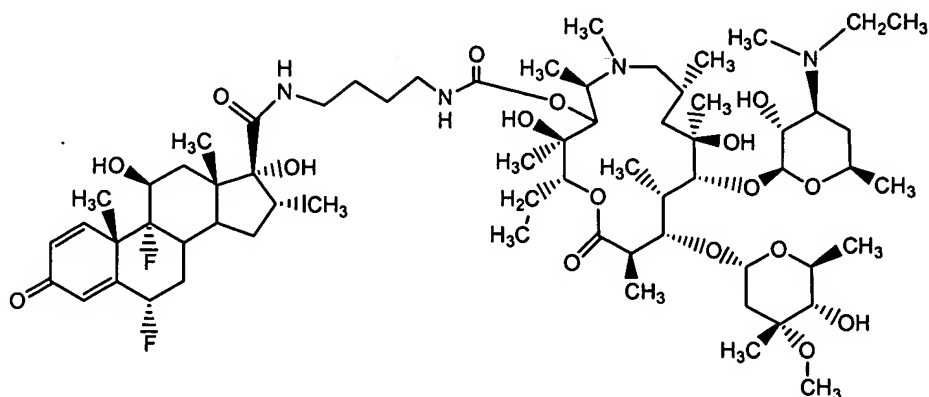
and pharmaceutically acceptable salts and solvates thereof.

21. (Currently amended) A compound of the formula



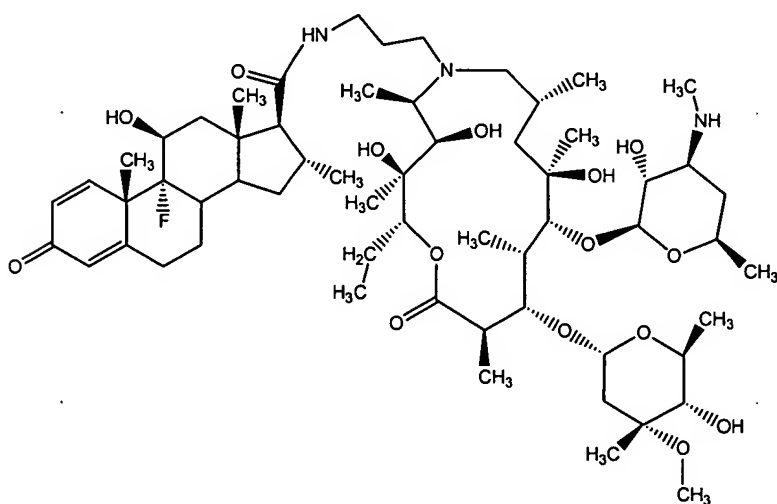
and pharmaceutically acceptable salts and solvates thereof.

22. (Currently amended) A compound of the formula



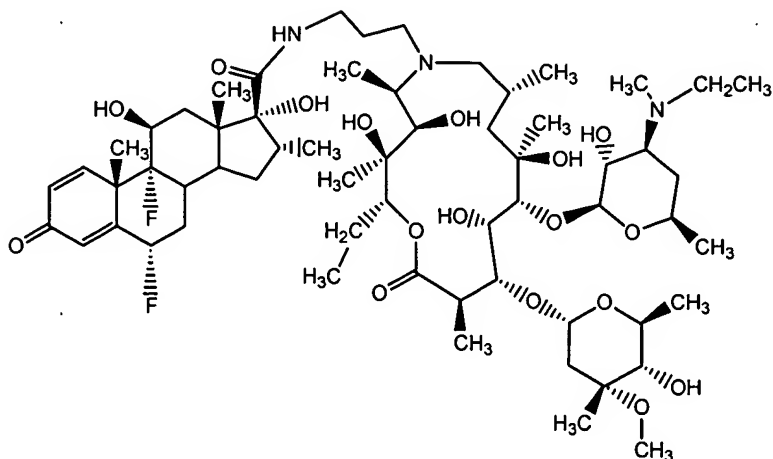
and pharmaceutically acceptable salts and solvates thereof.

23. (Currently amended) A compound of the formula



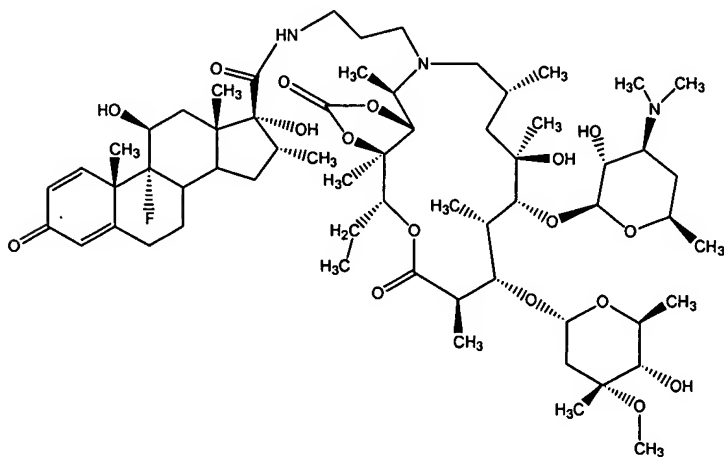
and pharmaceutically acceptable salts and solvates thereof.

26. (Currently amended) A compound of the formula



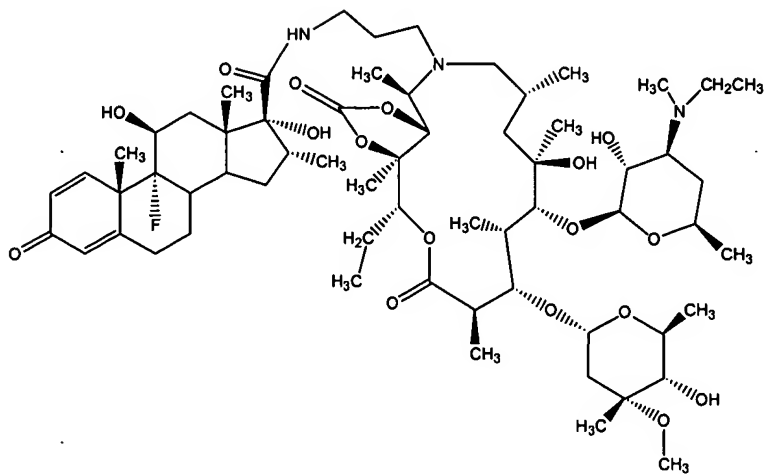
and pharmaceutically acceptable salts and solvates thereof.

27. (Currently amended) A compound of the formula



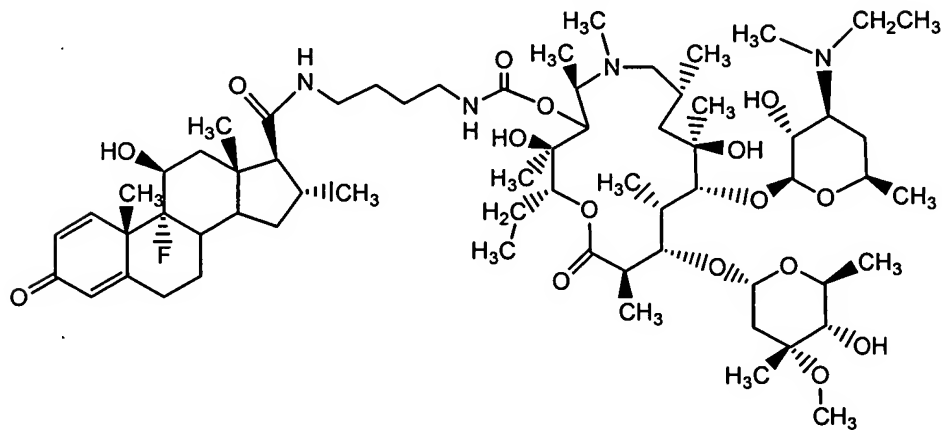
and pharmaceutically acceptable salts and solvates thereof.

28. (Currently amended) A compound of the formula



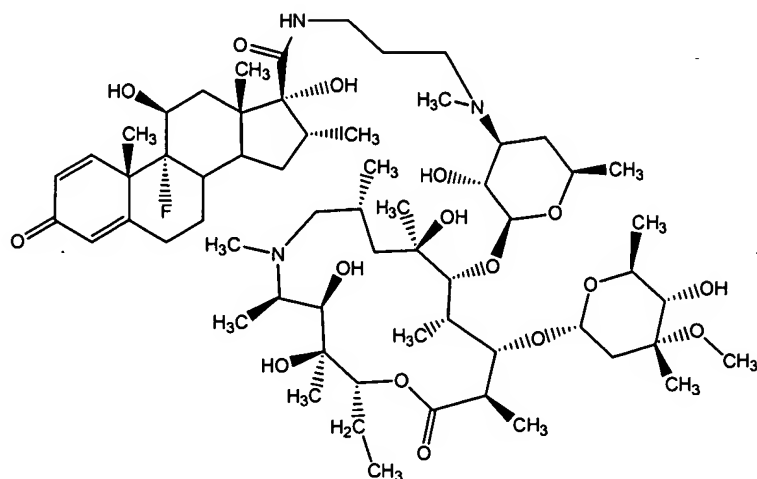
and pharmaceutically acceptable salts and solvates thereof.

29. (Currently amended) A compound of the formula



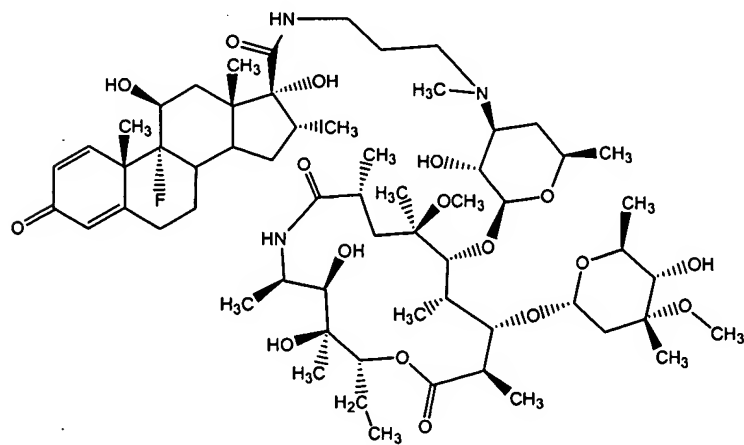
and pharmaceutically acceptable salts and solvates thereof.

30. (Currently amended) A compound of the formula



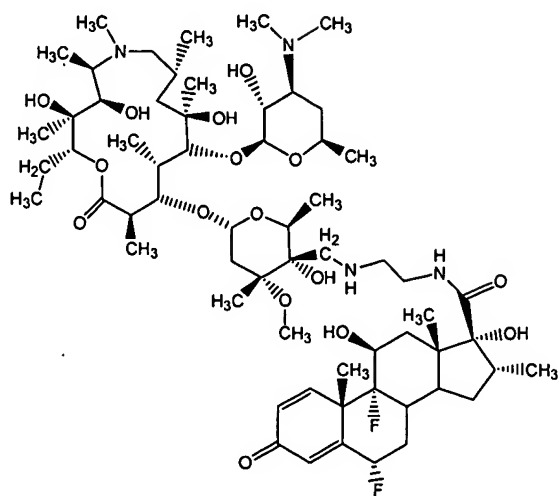
and pharmaceutically acceptable salts and solvates thereof.

31. (Currently amended) A compound of the formula



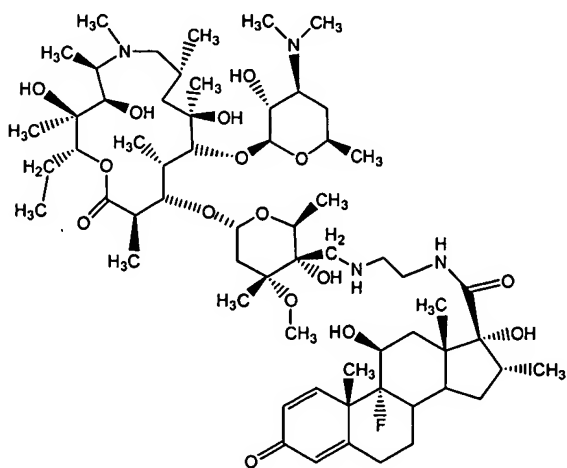
and pharmaceutically acceptable salts and solvates thereof.

32. (Currently amended) A compound of the formula



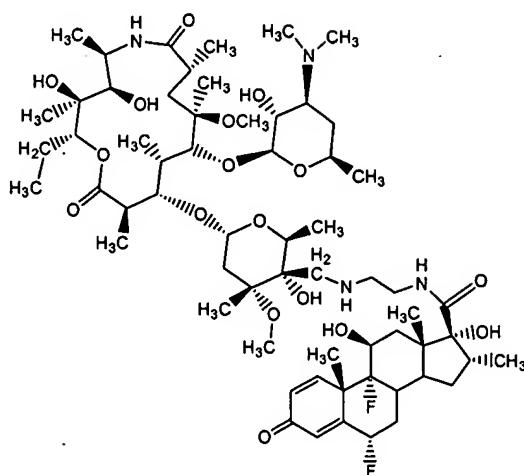
and pharmaceutically acceptable salts and solvates thereof.

33. (Currently amended) A compound of the formula



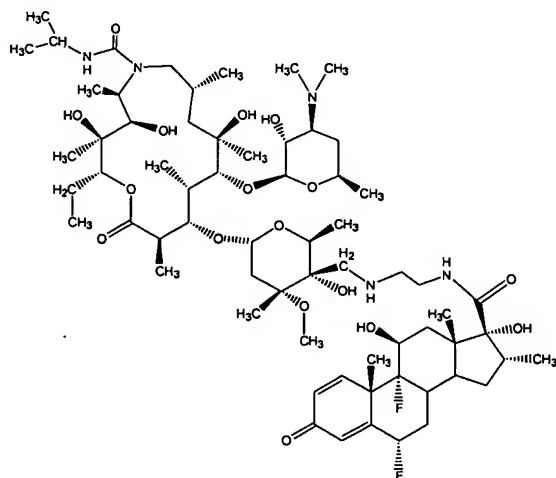
and pharmaceutically acceptable salts and solvates thereof.

34. (Currently amended) A compound of the formula



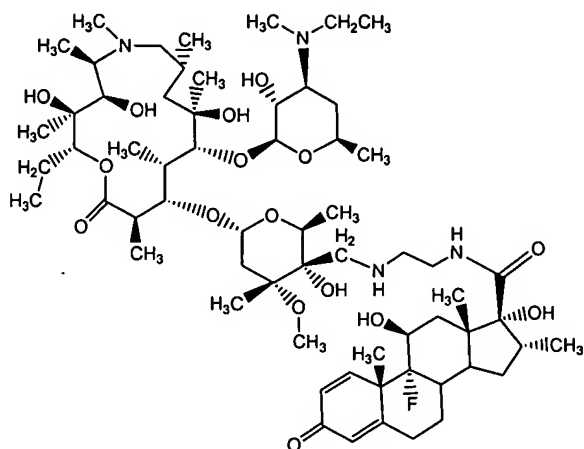
and pharmaceutically acceptable salts and solvates thereof.

35. (Currently amended) A compound of the formula



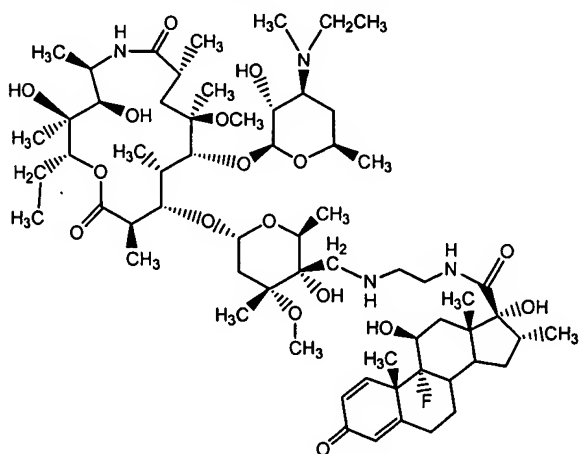
and pharmaceutically acceptable salts and solvates thereof.

36. (Currently amended) A compound of the formula



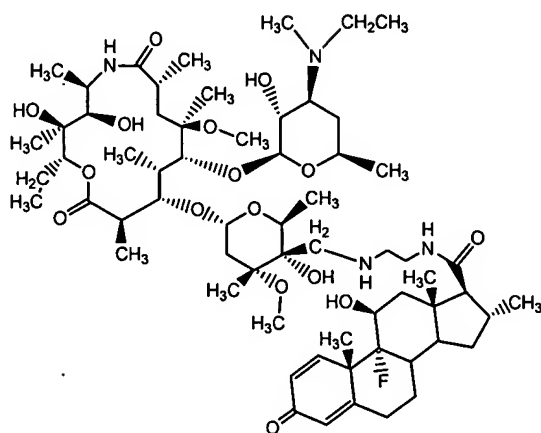
and pharmaceutically acceptable salts and solvates thereof.

37. (Currently amended) A compound of the formula



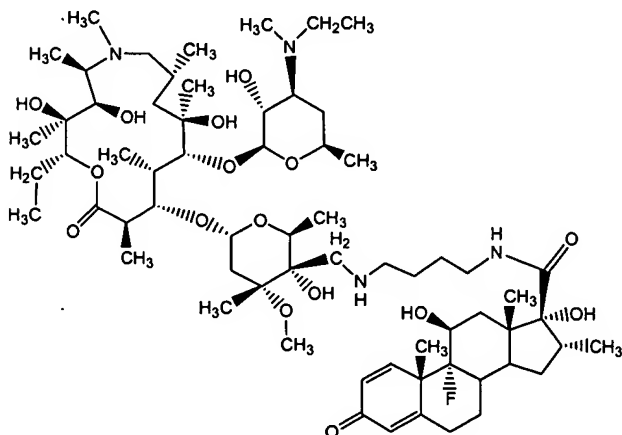
and pharmaceutically acceptable salts and solvates thereof.

38. (Currently amended) A compound of the formula



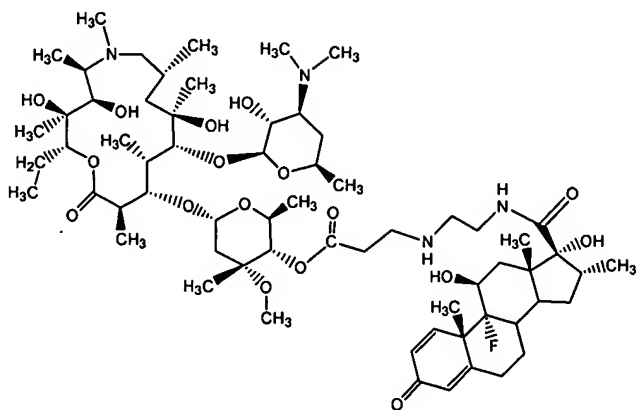
and pharmaceutically acceptable salts and solvates thereof.

39. (Currently amended) A compound of the formula



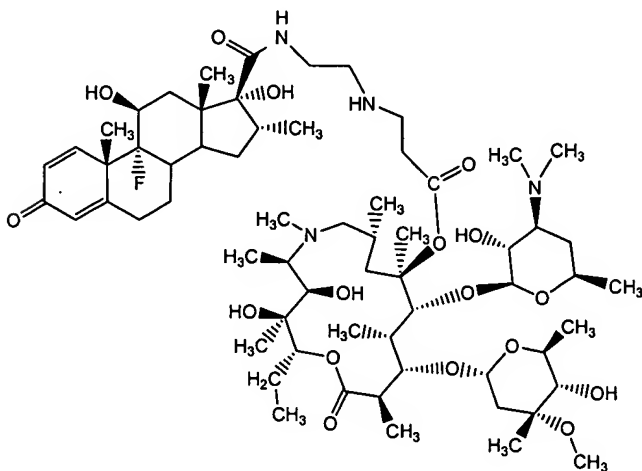
and pharmaceutically acceptable salts and solvates thereof.

40. (Currently amended) A compound of the formula



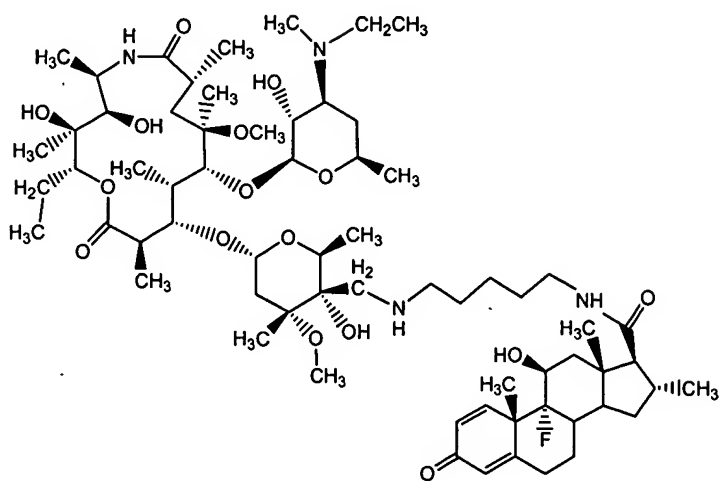
and pharmaceutically acceptable salts and solvates thereof.

41. (Currently amended) A compound of the formula



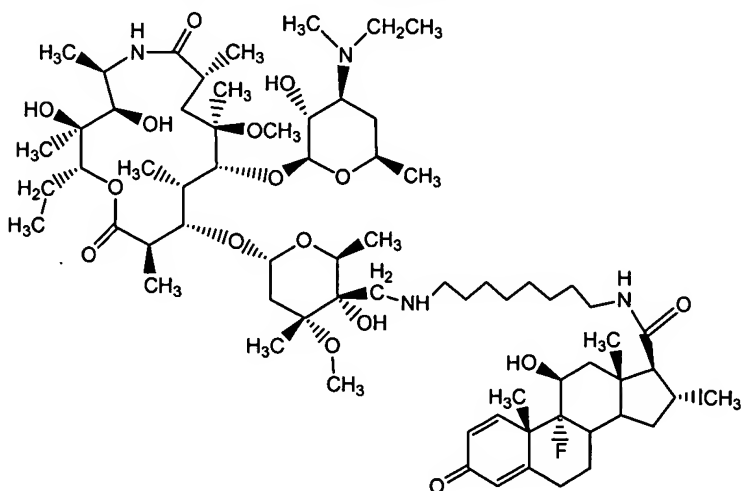
and pharmaceutically acceptable salts and solvates thereof.

42. (Currently amended) A compound of the formula



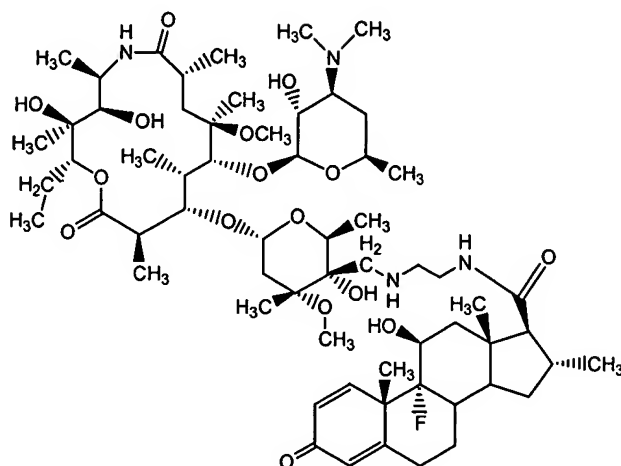
and pharmaceutically acceptable salts and solvates thereof.

43. (Currently amended) A compound of the formula



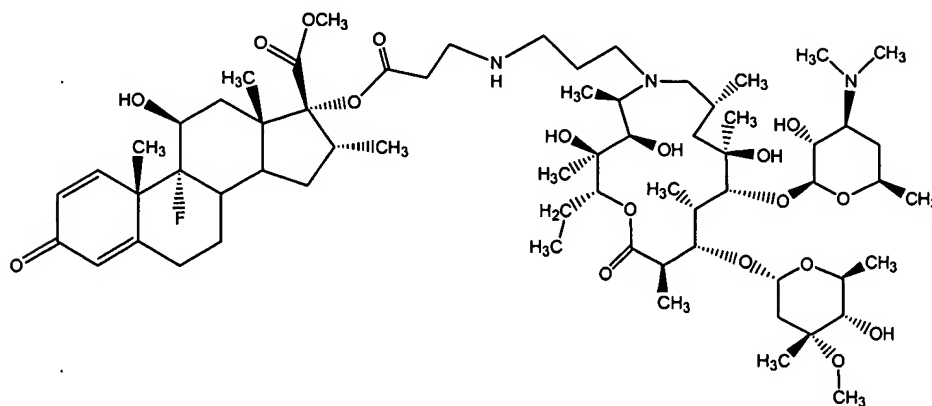
and pharmaceutically acceptable salts and solvates thereof.

44. (Currently amended) A compound of the formula



and pharmaceutically acceptable salts and solvates thereof.

45. (Currently amended) A compound of the formula



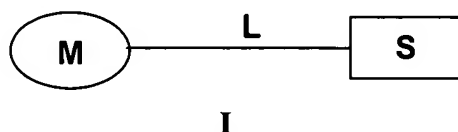
and pharmaceutically acceptable salts and solvates thereof.

-

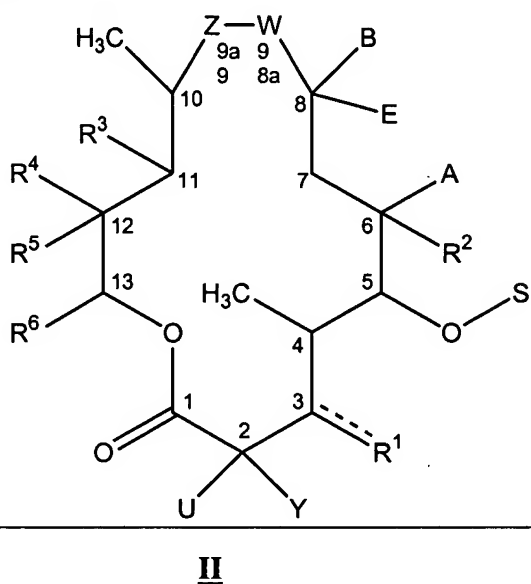
The chemical structure shows a steroid nucleus with a ketone at C3, a hydroxyl group at C14, and a methyl group at C10. A side chain at C13 includes a thioether linkage to a dimethylamino group, a ketone at C15, and a long alkyl chain ending in a tertiary amine. The alkyl chain is further substituted with a hydroxyl group, a methyl group, and a complex side chain including a thioether, an amide, and a long alkyl chain with a tertiary amine.

{W:\03818\100L650US1\00255565.DOC 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 }

48. (Currently amended) A process for the preparation for a compound of Formula I which comprises:



a) — for a compound represented by Formula I,
wherein **M** represents a group of Formula II:



wherein

(i) Z and W independently are $>C=O$, $>CH_2$, $>CH-NR_NR_S$, $>N-R_N$ or $>C=N-R_M$, wherein

R_t and R_s independently are hydrogen or alkyl;

R_M is hydroxy, alkoxy, substituted alkoxy or OR^p:

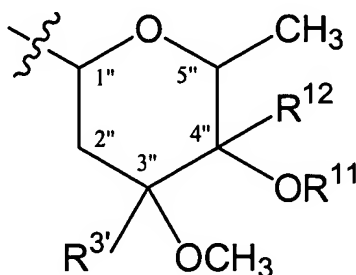
R_N is hydrogen, R^P, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or -C(X)-NR_tR_s; wherein X is =O or =S;

provided that Z and W cannot both simultaneously be, >C=O, >CH₂, >CH-NR_iR_s, >N-R_N, >C=N-R_M or a bond;

-
- Chemical structure of a substituted pyranose ring. The ring is a six-membered ring with an oxygen atom at the bottom. The carbons are numbered 1' to 5'. Substituents are: R^8 at C3', R^9 at C4', CH_3 at C5', R^{10} at C2' (via an oxygen atom), and a wavy line at C1'.

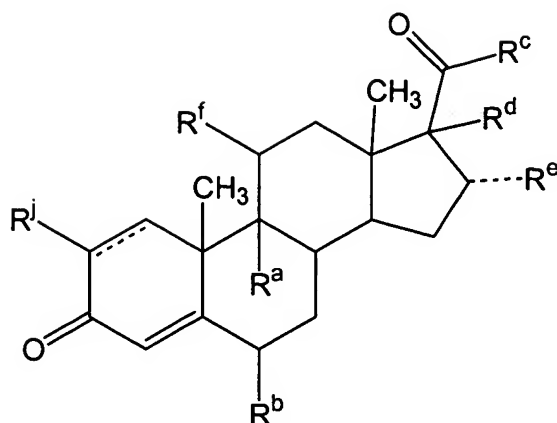
III

S² sugar moiety of Formula IV:



IV

R¹² is hydrogen or a group that with O-R¹¹ group and with C/4" carbon atom



X

wherein

R^a and R^b independently represents, hydrogen or halogen;

R^c is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;

R^d and R^e independently represents: hydrogen, hydroxy, methyl or C₁-C₄-alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

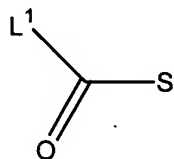
R^f is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

R^j is hydrogen or halogen;

or a pharmaceutically acceptable salt or solvate;

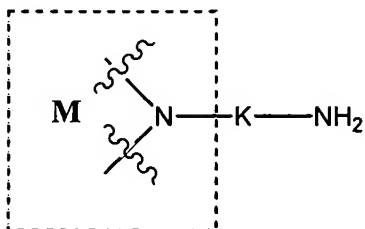
a) for a compound represented by Formula I comprising the steps of:

where X² is -NHC(O)-, by reacting a compound of Formula V:

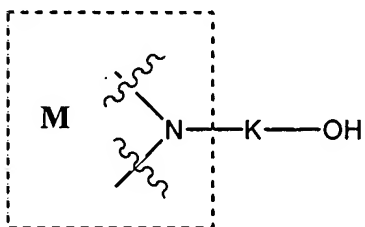


V

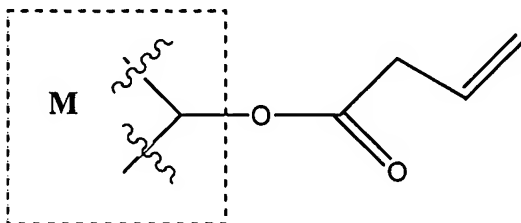
wherein L¹ represents a leaving group, and a free amino group of a macrolide represented by Formula **VIId**:



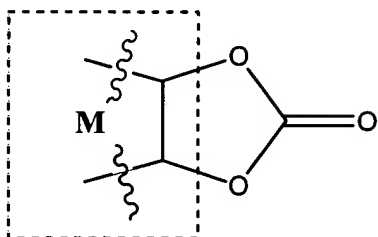
b) for a compound represented by Formula I, where X² is -OC(O)-, by reacting a compound of Formula V and a hydroxyl group of a macrolide represented by Formula VIe:



c) for a compound represented by Formula I, wherein X¹ is -OC(O)-, Q is NH and X² is -NHC(O)-, by reacting a macrolide represented by:

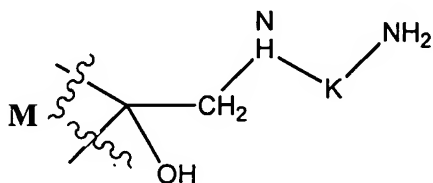

$$\text{H}_2\text{N}-\text{K}-\text{NH}-\text{C}(=\text{O})-\text{S}$$

d) for a compound represented by Formula I, where X¹ is -OC(O)NH- and X² is -NHC(O)-, by reacting a macrolide represented by Formula VII and a free amino group of Formula IVc:



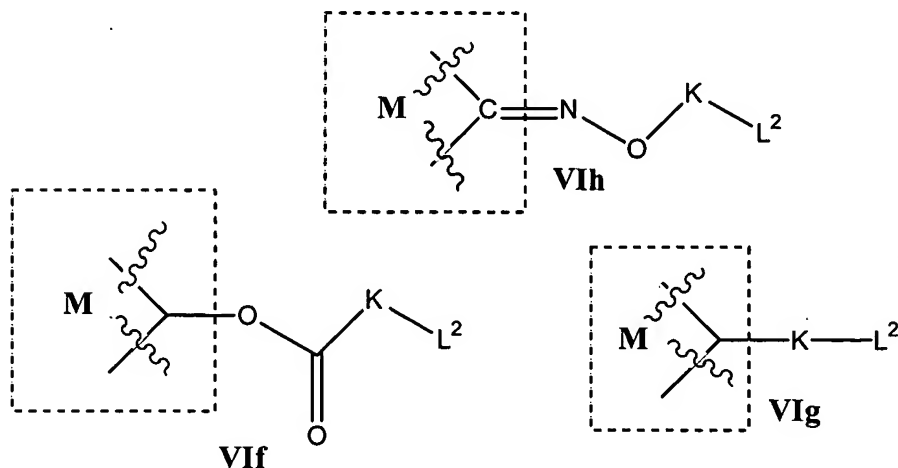
VII

e) for a compound represented by Formula I, where X^1 is $-\text{CH}_2-$, Q is $-\text{NH}-$ and X^2 is $-\text{NHC(O)}-$, by reacting a macrolide represented by Formula Va and a compound of Formula V:

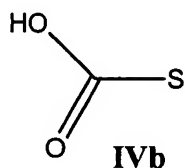


Va

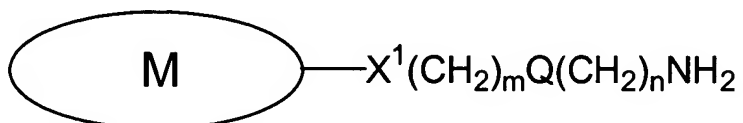
f) compound of Formula **I** by reacting a macrolide represented by Formula **VI**f or by Formula **VI**g or by Formula **VI**h having a leaving group L_2



with a free carboxyl acid of steroid represented by Formula IVb

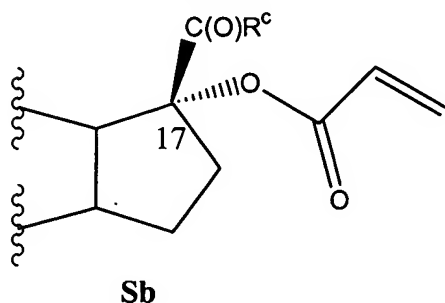


g) for a compound represented by Formula I, wherein X¹ is -OC(O)-, Q is NH and X² is -NH- by reacting a macrolide represented by:



VIId

and a steroid subunit having a -C=C- bond represented by Formula **Sb**:



following by modification of R^c group.

49. (Previously Presented) A pharmaceutical composition comprising a compound according to claim 1 and pharmaceutically acceptable salts or solvate thereof as well as pharmaceutically acceptable diluent or carrier.
50. (Previously Presented) A method of treatment of inflammatory diseases, disorders and conditions characterized by or associated with an undesirable inflammatory immune response, and all diseases and conditions induced by or associated with an excessive secretion of TNF- α and IL-1 which comprises administering to a subject a therapeutically effective amount of a compound according to claim 1.
51. (Currently amended) A method of treating inflammatory conditions and immune or anaphylactic disorders associated with infiltration of

